Pulmonary Alveolar Proteinosis

WE HAVE TREATED 14 patients with pulmonary alveolar proteinosis by lung lavage, some more than once. In each case, the initial treatment was given because the patient was progressively deteriorating and unable to work, or, in the case of two small children, cachetic and near death. In each case, lung lavage reversed the clinical course.

In 1968, I coauthored a paper on treatment of a patient with pulmonary alveolar proteinosis, whom I had seen in 1966 while on the staff at Stanford.[1] In this paper, we reported the physiological and radiological changes of that patient after left and right lung lavage. Chest roentgenograms, gas exchange and blood gas measurements before and after each lung lavage documented the improvement. The observations reported in this paper reflect the type of improvement that we have noted in the 13 other patients. By the evening of the lavage of the left lung (we always do the left first), findings on physical examination usually show greater expansion of that lung when contrasted with the expansion of the right lung. The patient may comment that the left side feels lighter. Findings on an x-ray film of the chest done on the afternoon or evening following left lung lavage are also very interesting. While the right lung retains its infiltrates, the left lung is in large part cleared of infiltrates. By the next day, the patients comment on their new-found breath as they walk around the ward or climb the hospital stairs. We know of few instances in medicine where the effects of therapy are so immediate and so striking, and have viewed lung lavage as being as specific for pulmonary alveolar proteinosis as penicillin is for pneumococcal pneumonia.

Since our observations differ so notably from those described in the Lewiston-Robin symposium in this issue of the JOURNAL, one might wonder if lung lavage is done differently by different groups. The whole lung lavage technique, as we do it, differs from the original description of Ramirez and co-workers[2] in several respects. A single lung lavage procedure consists of 12 to 15 lavages of the degassed lung of approximately 1 to 1½ liters normal saline solution, each taking approximately five minutes to carry out. Thus, we use approximately 20 liters of saline solution rather than the much smaller volume (approximately three liters) used by Ramirez and co-workers.[2] We do not find that addition of heparin or acetylcysteine to the saline solution makes the lavage more effective. We percuss during the lavage with a mechanical percussor. We take great pains to regenerate normal surface forces after the lavage before removing the Carlen's tube. The basis of each of these modifications and their details are described in Reference 3. Two of our former fellows have recently treated patients with pulmonary alveolar proteinosis at different hospitals using the procedure that we have described, and have obtained the gratifying results that have been our experience. I suspect that less successful results are due to lack of attention to detail which has been our concern.

The symposium suggests that lung lavage might result in lung damage. There is no question that lung lavage washes out surfactant from the lungs. We can see evidence for this by examining the size of the bubbles in the foam of the first lavage effluent as compared with subsequent ones. The first lavage effluent contains many uniformly small bubbles (approximately 0.1 mm) on the surface. Later effluents have larger bubbles on the surface with only a few small bubbles. The size of the surface bubbles is not related to the quantity of sediment. The reduction in numbers of stabile small bubbles must be secondary to the reduction in the quantity of surfactant in later lavages.

In recognition of this problem, we have always been concerned with the possibility that removal of the surfactant by the lavage procedure would result in a lung with reduced compliance when reinflated with air. Because of widely different compliances between the lavaged and gas exchange lung, the lung with lower compliance or greater recoil force (lavaged lung) would tend to become atelectatic while the lung with the higher compliance or lower recoil force (gas exchange lung) would develop compensatory overexpansion. Therefore, with the Carlen's tube still in place, we suction saline and then foam between ventilations of the lavaged lung. We measure the pressure-volume characteristics frequently. We continue this until the pressure-volume characteristics of the lavaged lung are the same as those of the gas exchange lung. This is usually the same compliance as that measured before the lavage procedure. We do not remove the Carlen's tube until the compliances of both lungs are the same. This takes approximately one hour from the time the lavage procedure is discontinued. This is evidence

that the normal surface forces can be rapidly regenerated after surfactant is washed off the surface lining of the lung. Several hours following lavage of the left lung, there is evidence, from the movement of each side of the chest, that the left lung has a higher compliance than the right lung. Gas exchange is also better by this time, as evidenced by a reduction in the alveolar-arterial oxygen difference. Thus, lung lavage as we do it does not appear to damage the lungs of patients with pulmonary alveolar proteinosis. Parenthetically, in a total of 40 lung lavages done on our 14 patients (in each patient two lavages were carried out, one for each lung; in some patients repeat lavages were required), a low-grade fever was observed only once and this lasted for only 24 hours. We do not give our patients antibiotics before or after the procedure.

Our longest follow-up is that of a 31-year-old woman in whom we carried out lavage at age 23 (1967) because of severe exertional dyspnea. The resting arterial oxygen pressure in this patient was 42 mm of mercury. After lung lavage, she was notably improved and arterial blood gases were normal; in fact, she felt normal and soon returned to work. One year later the patient returned to see us because of increasing symptoms. She asked to have another lavage procedure done. Consequently, we repeated it with the same results as were obtained during the preceding year. This happened two more times, the last being in 1971. Since that time, the patient has been in complete remission and able to work regularly. Four other patients had more than one lung lavage in our series, all at their request. Apparently, the disease process eventually smolders out. The objective of lung lavage should be to prevent the progressive deterioration of the patient's condition which may lead to a hypoxic death and to leave the patient asymptomatic after the disease process becomes quiescent. At this time we have no evidence that the lavaged patients will have a shortened life expectancy. This is important because this disease generally afflicts young people who are interested in obtaining life insurance policies. Life insurance companies have hesitated to insure them.

In the symposium, Dr. Robin suggests that pulmonary alveolar proteinosis is a disease which is now disappearing. Because pulmonary alveolar proteinosis is rare, any single physician might have a limited ability to evaluate its incidence. In contrast to Dr. Robin's observations, we are of the opinion that pulmonary alveolar proteinosis may be increasing in incidence. We have seen five new cases of pulmonary alveolar proteinosis in the past year. This represents a higher yearly new case rate than we have seen in the past. I do not think that Dr. Robin's or my experiences can be used to determine if the incidence of this disease is changing. Since it was suggested that the occurrence of the disease might be related to changes in the environment,[4] it would be appropriate for the Environmental Protection Agency to make this a reportable disease, thus establishing a registry for incidence and geographical location.

From the point of view of the patient's management, I would question the wisdom of the use of the term "secondary" pulmonary alveolar proteinosis to describe disorders of known cause just because there is some anatomical similarity to pulmonary alveolar proteinosis (Table 2 of the symposium). While these disorders might have alveoli filled with amorphous granular material, as seen in pulmonary alveolar proteinosis, they are usually associated with chronic inflammatory changes including fibrosis. To label these disorders as pulmonary alveolar proteinosis distorts their true cause and may be misleading to the understanding of the natural history and cause of pulmonary alveolar proteinosis. The hallmark of true pulmonary alveolar proteinosis is the presence of amorphous granular material in what otherwise appears to be normal alveoli, and minimal lung destruction, fibrosis and inflammation. It is this characteristic which renders it particularly susceptible to treatment by lung lavage techniques.

Finally, I would like to add to the bibliography on this subject the 1965 article by Larson and Gordinier[5] since it represents the largest review of reported cases. In spite of the fact that it was published ten years ago, it is extremely comprehensive and beautifully summarizes much of what we know about the disease today.

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